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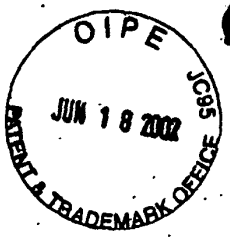


IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF: :

Yoshio Hayashi, et al. : EXAMINER: Nolan, P.

SERIAL NO. : 09/499,765 :

FILED: February 8, 2000 : GROUP ART UNIT: 1644

FOR: Composition containing α-fodrin or α-fodrin fragment protein

DECLARATION UNDER 37 C.F.R. 1.132

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

SIR:

Now comes Yoshio Hayashi who deposes and states that:

1. I am a Professor of Department of Pathology, Tokushima University School of Dentistry located at Tokushima Prefecture in Japan. I have been working for 20 years in the field of the research of autoimmune diseases, especially Sjogren Syndrome.

2. I am one of the inventors of the present application.

3. The following experiment was carried out by me or under my direct supervision and control in order to investigate the inhibitory effect of human α-fodrin fragment protein on the on-going Sjogren Syndrome.

(1) Test product:

The inhibitory effect on the ongoing Sjogren Syndrome was carried out by using the human α-fodrin fragment protein, which is the glutathione S-transferase-α-fodrin fragment protein fusion

protein, obtained in accordance with Example 2 of the present specification.

(2) Test method;

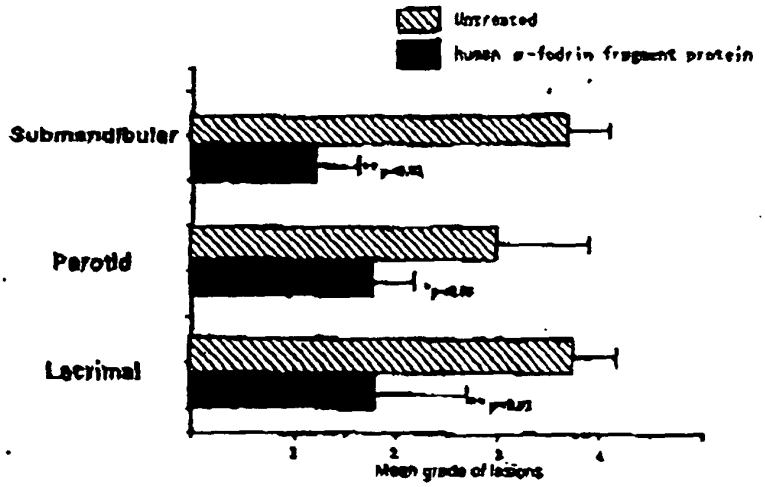
Test method was carried out according to a procedure similar to that described in Example 4 of the present specification.

That is, NFS/sld mice, 4, 5, 6, and 7 weeks after operation at postnatal day 3 (3d-TX), were intravenously dosed with a saline solution (25 μg/0.1 ml) of the glutathione S-transferase-α-fodrin fragment protein fusion protein or, as untreated control, of glutathione S-transferase (Mice examined n= 5, 20 μg/week/head iv).

The mice were autopsied 8 weeks after the operation at postnatal day 3, and the mean grade of lesions was assessed by the method of White and Casarett using pathological indicators [Journal of Immunology, 112, p178(1974)].

(3) The results are shown in the following.

Mean grade of lesions in NFS/sld mouse administered with the human α-fodrin fragment protein



3d-TX NFS/sld mice provide a known murine model of Sjogren Syndrome (The Journal of Immunology, 1994, 153:2769). It is known that (i) growth of lesions in the submandibular, parotid and lacrimal glands in these mice is indicative of Sjogren Syndrome, and (ii) significant symptoms of Sjogren Syndrome are first found after '4-weeks', in the said models ('Result' and 'Figure 1' in p2770-2771 of the above Journal). Therefore, results of treatment after 4, 5, 6, and 7-weeks in the said 3d-TX NFS/sld mice models indicate an efficacy against an ongoing Sjogren Syndrome.

The results of this experiment show that administration of the human α-fodrin fragment protein to 3d-TX NFS/sld mice inhibited the growth of lesions in the submandibular, parotid and lacrimal glands. That is, treatment with human α-fodrin fragment protein after '4-weeks' inhibited the symptoms of Sjogren Syndrome.

In contrast, the control mice that received only glutathione S-transferase, exhibited lesion growth.

The results demonstrated above, and in Example 4 of the patent application, confirm that treatment with the human α-fodrin fragment protein (obtained in accordance with Example 2) has a suppressive effect on ongoing and onset of Sjogren Syndrome.

Thus, the human α-fodrin fragment protein described in the present application and obtained through the methods described in Example 2 therein is a useful prophylactic and therapeutic agent for autoimmune disease, particularly Sjogren Syndrome.

4. It is declared by the undersigned that all statements made herein of undersigned's own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with th knowledge

that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Yoshio Hayashi

Yoshio Hayashi, D.D.S., Ph.D.

This 13 day of June, 2002
Tokushima, Japan